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Effects of airway obstruction induced by asthma attack on particle deposition

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ABSTRACT

Two computational models of the airway tree up to six generations deep were reconstructed from computed tomography scans from a single patient. The first scan was taken a day after an acute asthma episode while the second scan was taken 30 days later when the patient had recovered. The reconstructed models were used to investigate the effects of acute asthma on realistic airway geometry, the airflow patterns, the pressure drop, and the implications it has on targeted drug delivery. Comparisons in the geometry found that in general the average increase in diameter was larger in the right airway the airway is larger in diameter than the left side. The average airway branch difference from the Asthma Model to the Recovered Model was found to be 10.4% in the right airway and 4.8% in the left airway; however the airway dilation during the recovery stage was not consistent through the entire branch airway. Instead there were local branches that exhibited a very high local dilation recovery ($\approx 30\%$ recovery). This inconsistent dilation recovery makes it difficult to predict where and how much each branch will recover from an asthma episode. In terms of targeted drug delivery studies in the lung airways, the deposition patterns will be under-predicted for airway models that are reconstructed from a healthy or non-asthma affected lung airway. The discrepancy may reach as high as 13% between the two models for particles $\geq 10\,\mu m$ under a turbulent flow. For particles $< 10\,\mu m$, the discrepancy reduces to 1% as the particle size reduces to $1\,\mu m$ under a turbulent flow. This means that drug delivery studies in the lung airway should consider the effects of airway narrowing and that if a recovered or a healthy airway is used, then the deposition fraction and efficiencies are expected to be under-predicted.

1. Introduction

Acute asthma manifests itself most commonly as wheezing, coughing, chest tightness, shortness of breath, and sputum production. Causes of asthma have been attributed to many factors including the inhalation of allergens and toxic particles found in the surrounding environment. The treatment of asthma is often reliant on aerosolised beta-adrenergics, parasympatholytics, and corticosteroids which are delivered into the airways through nebulisers or metered-dose inhalers. However the targeted drug delivery is not efficient. Currently marketed inhalation therapies can only deliver an effective inhalation of 10–20% of a drug load into the lung (Clark, 1995) while Roland, Bhalla, and Earis (2004) reviewed that the

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extra drug load (80–90%, the rest of the drug) in certain drugs may in fact cause side effects to the patient. Since particles are transported by the inhaled air, studies of the airflow mechanisms and patterns within the airway can provide data that is pertinent to the prediction of gas-particle flows and regional tissue exposure to contaminated air and other clinical respiratory research.

The earliest studies of airflow in the lung airways was the experimental work by Schroter and Sudlow (1969). A few velocity profiles and flow patterns were presented for a double-bifurcation model. In other experimental studies the central airway up to the third generation of the bifurcation was used (Chang & El Masry, 1982; Isabey & Chang, 1981). It was concluded that flow patterns were most likely dependent on the airway geometry. In the above studies, the respiratory flow was treated as a steady or quasi-steady condition based on the Womersley parameter for normal breathing. Airflow patterns change as a result of an acute asthma episode where the combination of bronchospasm, mucus plugging, and mucosal edema build up leads to increased airway resistance as the diameters of the airways are reduced. Experimental studies with human subjects have shown that patients with asthma produce different particle deposition patterns (Chalupa, Morrow, Oberdorster, Utell, & Frampton, 2004; Martonen, Fleming, Schroeter, Conway, & Hwang, 2003; Sbirlea-Apiou et al., 2004). Since the nature of *in vivo* studies can be invasive many alternate studies make use of replica and computational models. However most of these studies have considered airflow patterns affected by tumours, airway constrictions and airway blockage associated with chronic obstructive pulmonary disease (COPD) in local subregions of the lung airways. For example, Kim and Kang (1997a) studied local deposition efficiencies and deposition patterns of ultrafine particles in a sequential bifurcation tube model in normal airways and with obstructive airway disease; Musante and Martonen (2001) investigated the effects of both sidewall and carinal tumours on a single symmetric bifurcation under sedentary conditions; Zhang, Kleinstreuer, Kim, and Hickey (2002) studied the airflow and deposition of micron-size particles in a triple lung bifurcation affected by sidewall tumours in generations G3–G6; Yang, Liu, and Luo (2006) demonstrated the importance of the boundary conditions within a locally obstructed airway (generations G5–G8); and Farkas and Balásházy (2007) simulated the effect of local obstructions and blockage on the deposition of aerosols in the lung airway subregion of G3–G5. The work by Longest, Vinchurkara, and Martonen (2006) however, included double bifurcation models of upper (G3–G5) and central (G7–G9) airways for a four-year-old child where the effects of asthma was modelled as a 30% constriction of the airway branches. Additional studies in obstructed airways (Kim, Brown, Lewars, & Sackner, 1983; Kim, Eldridge, Garcia, & Wanner, 1989; Kim, 1989; Kim & Kang, 1997b), showed that greater deposition occurred in the obstructed lung compared with a normal lung.

In the above studies, lung subregions of interest were reconstructed from Weibel's (1963) model and airway constrictions were modelled by decreasing the airway diameters. This paper extends these ideas by reconstructing two computational models of the tracheobronchial airway tree down to the sixth generation from computed tomography (CT) scans of a single patient. The first scan was taken a day after an acute asthma episode while the second scan was taken 30 days later when the patient had recovered. Comparisons between the two models are made in terms of (i) the geometric changes in the airway and (ii) the significance of the airway geometry change on the airflow patterns and particle deposition. Since the intention of drug delivery studies is to better understand and deliver drug particles more efficiently, the results of this comparative model study can help determine whether using a single recovered or non-asthmatic airway model is sufficient for drug delivery studies or whether the model indeed needs to be reconstructed from an asthma-affected patient. In addition some of the data can help to reveal what scales of magnitudes exist in the airway recovery 30 days after the onset of asthma.

While most deposition studies have used Weibel's (1963) model and considered the bifurcation airways as symmetric, the use of realistic models then leads to a lack of exact matching of comparative/compatibility studies as the data does not necessarily exist in the literature unlike the data for Weibel's model. The authors have adopted the method by Luo and Liu (2009) which compared their CFD model against (de Rochefort et al., 2007)'s experimental data, the method by van Ertbruggen, Hirsch, and Paiva (2005) which compared their CFD model against (Calay, Kurujareon, & Holdo, 2002)'s numerical predictions, and the method by Choi, Tu, Li, and Thien (2007) which compared with Schlesinger, Gurman, and Lippmann (1982) and Kim and Fisher (1999)'s data. This paper follows the same approach in conducting comparisons of CFD with the available data. The results in this paper are not intended to be a generalization but rather to contribute towards establishing data for future comparative benchmarks such as the work by Calay et al. (2002), and to present the modelling requirements, techniques, and different analysis methods. For generalised findings, the use of a general model such as the standard Weibel model is a common method for deposition studies (Hofmann, Golser, & Balashazy, 2003; Longest & Vinchurkar, 2009). The use of a large number of models has only been performed by De Backer et al. (2008) which used 14 models to produce a general trend to detect changes in airway resistance in asthmatics.

2. Method

2.1. CT scans and image segmentation

The first two models were developed from CT scans from a 66-year-old non-smoking, asthmatic male (height 171 cm and weight 58 kg) using a helical 64 slice multidetector row CT scanner (General Electric) the day after hospital admission with an acute exacerbation of asthma. At the time, his lung function by spirometry (Spirocard, QRS Diagnostic, Plymouth,